Claims

1. A method of isolating a DNA encoding a peptide capable of acting as an agonist, antagonist or inverse agonist for an aimed receptor, which comprises the following steps (1) to (5):

(1) transfecting a cDNA or a DNA derived from a chromosome into a cell line derived from an endocrine cell to obtain a transformant;

(2) culturing the transformant of the above (1) to express the transfected DNA and contacting a culture supernatant, a cell extract or a membrane fraction of the transformant or the transformant *per se* with a cell where the aimed receptor is expressed;

(3) detecting a response reaction of the cell on the basis of the receptor;

(4) selecting a transformant where the culture supernatant, the cell extract or the membrane fraction of the transformant or the transformant *per se* shows the aimed activity; and

(5) identifying the DNA transfected in the transformant of the above (4) as a DNA for giving the aimed activity to the transformant.

2. A method of isolating a DNA encoding a peptide acting capable of as an agonist, antagonist or inverse agonist for an aimed receptor, which comprises the following steps (1) to (7):

(1) dividing a cDNA library prepared using an expression vector into pools each having 1 to 10,000 clone(s);

(2) transfecting a mixture of cDNA clones derived from each pool into a cell line derived from an endocrine cell to obtain a transformant;

(3) culturing the transformant of the above (2) for each pool to express the transfected cDNA and then contacting a culture supernatant, a cell extract or a membrane fraction of the transformant or the transformant *per se* for each pool with a cell where the aimed receptor is expressed;

(4) detecting a response reaction of the cell on the basis of the receptor for each pool;

(5) selecting a pool where the culture supernatant, cell extract or membrane fraction of the transformant or the transformant *per se* shows the aimed activity and dividing the selected pool into smaller pools than those in (1);

(6) repeating the operations of (2) to (5) until each pool consists of 1 clone; and

(7) identifying the cDNA which gives the aimed activity to the transformant.

3. The method of isolating a DNA according to claim 1 or 2, wherein the cDNA or the gene derived from a chromosome is a gene encoding an active peptide precursor.

4. The method of isolating a DNA according to claim 1 or 2, wherein the receptor is a G-protein coupled receptor.

5. The method of isolating a DNA according to claim 4, wherein the G-protein coupled receptor is an orphan G-protein coupled receptor.

6. The method of isolating a DNA according to claim 1 or 2, wherein the cell line derived from an endocrine cell is a cell line derived from an endocrine cell where the large T antigen gene of SV40 is expressed.

7. The method of isolating a DNA according to claim 1 or 2, wherein the cell line derived from an endocrine cell is a cell line derived from an endocrine cell where the large T antigen gene of temperature-sensitive mutant strain of SV40 is expressed.

8. The method of isolating a DNA according to claim 1, 2, 6 or 7, wherein the cell line derived from an endocrine cell is a cell line derived from a cell of a non-human transgenic animal.

9. The method of isolating a DNA according to claim 8, wherein the non-human transgenic animal is a transgenic rat.

10. The method of isolating a DNA according to claim 7, wherein the temperature-sensitive mutant strain of SV40 is SV40tsA58.

11. The method of isolating a DNA according to claim 1, 2, 6, 7 or 8, wherein the cell line derived from an endocrine cell is a cell line derived from hypothalamus or Langerhans islets.

12. The method of isolating a DNA according to claim 1, 2, 6, 7 or 8, wherein the cell line derived from an endocrine cell is a cell derived from hypothalamus where at least one gene selected from the group consisting of leptin receptor (Ob-Rb) gene, preproneuromedin U gene, RFamide-related peptide (RFRP) preproprotein gene, preproorexin gene, preproopiomelanocortin gene, preproneuropeptide Y gene, preproneuropeptide FF gene, preprocorticotropin-releasing hormone gene, preprothyrotropin-releasing hormone gene, preproghrelin gene, prepromelanin concentration hormone gene, cocaine- and amphetamine-regulated transcript (CART) gene, type 2 neuromedin U receptor (NMU2R) gene, RFRP receptor gene, type 4 melanocortin receptor (MC4R) gene, type 1 neuropeptide Y receptor (NPY1R) gene, type 5 neuropeptide Y receptor (NPY5R) gene, type 2 neuropeptide FF receptor (NPFF2) gene, type 1 corticotropin-releasing hormone receptor (CRHR-1) gene, type 2 corticotropin-releasing hormone receptor (CRHR-2) gene, ghrelin receptor gene, type 1 melanin concentration hormone receptor (MCHR1) gene, preproagouti-related peptide gene, sulfonylurea receptor gene, ciliary neurotrophic factor (CNTF) receptor gene, type 1 neuromedin U receptor (NMU1R) gene, type 1 orexin receptor (OX1R) gene, type 2 orexin receptor (OX2R) gene, type 1 angiotensin II receptor gene, galanin receptor, glucagon-like peptide-1 (GLP-1) receptor gene and glucagon-like peptide-2 (GLP-2) receptor gene is endogenously

expressed.

13. The method of isolating a DNA according to claim 1, 2, 6, 7 or 8, wherein the cell line derived from an endocrine cell is a cell derived from hypothalamus where at least one peptide selected from the group consisting of leptin receptor (Ob-Rb), neuromedin U, RFamide-related peptide (RFRP) protein, orexin, opiomelanocortin, neuropeptide Y, neuropeptide FF, corticotropin-releasing hormone, thyrotropin-releasing hormone, ghrelin, melanin concentration hormone, cocaine- and amphetamine-regulated transcript (CART), type 2 neuromedin U receptor (NMU2R), RFRP receptor, type 4 melanocortin receptor (MC4R), type 1 neuropeptide Y receptor (NPY1R), type 5 neuropeptide Y receptor (NPY5R), type 2 neuropeptide FF receptor (NPFF2), type 1 corticotropin-releasing hormone receptor (CRHR-1), type 2 corticotropin-releasing hormone receptor (CRHR-2), ghrelin receptor, type 1 melanin concentration hormone receptor (MCHR1), agouti-related peptide, sulfonylurea receptor, ciliary neurotrophic factor (CNTF) receptor, type 1 neuromedin U receptor (NMU1R), type 1 orexin receptor (OX1R), type 2 orexin receptor (OX2R), type 1 angiotensin II receptor, galanin receptor, glucagon-like peptide-1 (GLP-1) receptor, glucagon-like peptide-2 (GLP-2) receptor and endorphin is endogenously expressed.

14. The method of isolating a DNA according to claim 1, 2, 6, 7 or 8, wherein the cell of the cell line an endocrine

cell is a cell derived from Langerhans islets where at least one gene selected from the group consisting of preproinsulin gene, prepro-glucagon gene, preprosomatostatin gene, prepropancreatic polypeptide gene, prohormone convertase 1 (PC1) gene, prohormone convertase 2 (PC2) gene, glucagon-like peptide-1 (GLP-1) receptor gene, PDX1 (pancreatic-duodenal homeobox 1) gene, Pax 4 gene, Pax 6 gene, neurogenin 3 gene, neuro D gene, Nkx 2.2 gene, Nkx 6.1 gene, glucokinase gene, type 2 glucose transporter gene, beta-cellulin gene, sulfonylurea gene, $P2Y_1$ receptor gene, glucagon-like peptide-1 (GLP-1) receptor gene, type 1 somatostatin receptor gene, type 2 somatostatin receptor gene, type 3 somatostatin receptor gene, type 4 somatostatin receptor gene, type 5 somatostatin receptor gene, insulin receptor gene, glucose transporter gene and nestin gene is endogenously expressed.

15. The method of isolating a DNA according to claim 1 or 2, wherein the cell in which the receptor is expressed is a B-cell line which is adapted for serum-free culture and in which the EBNA-1 gene of Epstein-Barr virus is expressed, where at least one of the following (1) to (3) is integrated in chromosomal DNA:

(1) DNA construct for expression of a transcription factor necessary for construction of an inducible expression system;

(2) DNA construct where a reporter gene is ligated at the downstream area of promoter having a responsive element

of a transcription factor; and

(3) DNA construct for expression of Gα protein or chimeric Gα protein.

16. The method of isolating a DNA according to claim 15, wherein the B-cell line is a Namalwa cell adapted for serum-free culture.

17. The method of isolating a DNA according to claim 16, wherein the Namalwa cell adapted for serum-free culture is Namalwa KJM-1 cell.

18. The method of isolating a DNA according to claim 15, wherein the transcription factor necessary for construction of the inducible expression system is a chimeric protein of a ligand binding domain of estrogen receptor and yeast Gal4p.

19. The method of isolating a DNA according to claim 15, wherein the responsive element of the transcription factor is cAMP responsive element (CRE), TPA responsive element (TRE), NFAT (nuclear factor of activated T cells) responsive element or serum responsive element (SRE).

20. The method of isolating a DNA according to claim 15, wherein the reporter gene is firefly luciferase gene, *Renilla reniformis* luciferase gene, chloramphenicol acetyltransferase gene, β-galactosidase gene, β-lactamase gene or green fluorescent protein gene.

21. The method of isolating a DNA according to claim 15, wherein the Gα protein is at least one Gα protein selected from

the group consisting of $G\alpha_{16}$, $G\alpha_{15}$, $G\alpha_q$, $G\alpha_{11}$, $G\alpha_s$, $G\alpha_i$, $G\alpha_o$, $G\alpha_z$, $G\alpha_{12}$, $G\alpha_{13}$, $G\alpha_{gust}$, $G\alpha_t$ and $G\alpha_{14}$.

22. The method of isolating a DNA according to claim 15, wherein the chimeric Gα protein is at least one chimeric Gα protein selected from the group consisting of the following (1) to (20):

(1) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_q$;

(2) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_i$;

(3) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_o$;

(4) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_z$;

(5) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_{12}$;

(6) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_{13}$;

(7) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_{Gust}$;

(8) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_t$;

(9) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_{14}$;

(10) chimeric Gα protein where C-terminal 5 amino acids

of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_{16}$;

(11) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_s$;

(12) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_i$;

(13) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_o$;

(14) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_z$;

(15) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_{12}$;

(16) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_{13}$;

(17) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_{Gust}$;

(18) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_t$;

(19) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_{14}$; and

(20) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_{16}$.

23. The method of isolating a DNA according to claim 15, wherein the transcription factor necessary for construction of the inducible expression system is a chimeric protein of

a ligand binding domain of estrogen receptor and yeast Gal4p, the promoter having a responsive element of the transcription factor is a promoter having a cAMP responsive element (CRE) and the reporter gene is firefly luciferase gene or *Renilla reniformis* luciferase gene.

24. The method of isolating a DNA according to claim 15, wherein the transcription factor necessary for construction of the inducible expression system is the chimeric protein of the ligand binding domain of estrogen receptor and yeast Gal4p, the promoter having a responsive element of the transcription factor is a promoter having a cAMP responsive element (CRE), the reporter gene is firefly luciferase gene or *Renilla reniformis* luciferase gene and the chimeric Gα protein is a chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_q$ or a chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_i$.

25. The method of isolating a DNA according to claim 1 or 2, wherein the response reaction of the cell is at least one response reaction selected from the group consisting of liberation of arachidonic acid, liberation of acetylcholine, increase of intracellular Ca^{2+}, production of intracellular cAMP, decrease of intracellular cAMP, production of intracellular cGMP, production of inositol phosphate, change in cell membrane potential, phosphorylation of intracellular protein,

activation of c-fos, change in intracellular pH, cell growth, expression level of reporter gene and expression level of marker gene.

26. The method of isolating a DNA according to claim 1 or 2, wherein the contact to the cell expressing the aimed receptor is a contact by layering of the cell onto a transformant.

27. A cell line derived from hypothalamus where at least one gene selected from the group consisting of leptin receptor (Ob-Rb) gene, preproneuromedin U gene, RFamide-related peptide (RFRP) preproprotein gene, preproorexin gene, preproopiomelanocortin gene, preproneuropeptide Y gene, preproneuropeptide FF gene, preprocorticotropin-releasing hormone gene, preprothyrotropin-releasing hormone gene, preproghrelin gene, prepromelanin concentration hormone gene, cocaine- and amphetamine-regulated transcript (CART) gene, type 2 neuromedin U receptor (NMU2R) gene, RFRP receptor gene, type 4 melanocortin receptor (MC4R) gene, type 1 neuropeptide Y receptor (NPY1R) gene, type 5 neuropeptide Y receptor (NPY5R) gene, type 2 neuropeptide FF receptor (NPFF2) gene, type 1 corticotropin-releasing hormone receptor (CRHR-1) gene, type 2 corticotropin-releasing hormone receptor (CRHR-2) gene, ghrelin receptor gene, type 1 melanin concentration hormone receptor (MCHR1) gene, preproagouti-related peptide gene, sulfonylurea receptor gene, ciliary neurotrophic factor (CNTF) receptor gene, type 1 neuromedin U receptor (NMU1R) gene, type

1 orexin receptor (OX1R) gene, type 2 orexin receptor (OX2R) gene, type 1 angiotensin II receptor gene, galanin receptor gene, glucagon-like peptide-1 (GLP-1) receptor gene and glucagon-like peptide-2 (GLP-2) receptor gene is endogenously expressed.

28. A cell line derived from hypothalamus where at least one peptide selected from the group consisting of leptin receptor (Ob-Rb), neuromedin U, RFamide-related peptide (RFRP) protein, orexin, opiomelanocortin, neuropeptide Y, neuropeptide FF, corticotropin-releasing hormone, thyrotropin-releasing hormone, ghrelin, melanin concentration hormone, cocaine- and amphetamine-regulated transcript (CART), type 2 neuromedin U receptor (NMU2R), RFRP receptor, type 4 melanocortin receptor (MC4R), type 1 neuropeptide Y receptor (NPY1R), type 5 neuropeptide Y receptor (NPY5R), type 2 neuropeptide FF receptor (NPFF2), type 1 corticotropin-releasing hormone receptor (CRHR-1), type 2 corticotropin-releasing hormone receptor (CRHR-2), ghrelin receptor, type 1 melanin concentration hormone receptor (MCHR1), agouti-related peptide, sulfonylurea receptor, ciliary neurotrophic factor (CNTF) receptor, type 1 neuromedin U receptor (NMU1R), type 1 orexin receptor (OX1R), type 2 orexin receptor (OX2R), type 1 angiotensin II receptor, galanin receptor, glucagon-like peptide-1 (GLP-1) receptor, glucagon-like peptide-2 (GLP-2) receptor and endorphin is endogenously expressed.

29. The cell line according to claim 27 or 28, wherein the cell line is a cell line in which the large T antigen gene of SV40 is expressed.

30. The cell line according to claim 27 or 28, wherein the cell line is a cell line in which the large T antigen gene of temperature-sensitive mutant strain of SV40 is expressed.

31. The cell line according to any of claims 27 to 30, wherein the cell line is a cell line derived from a non-human transgenic animal cell.

32. An immortalized cell line obtained from Langerhans islets or hypothalamus of a non-human transgenic animal transfected with the large T antigen gene of temperature-sensitive mutant strain of SV40.

33. The cell line according to claim 32, wherein the immortalized cell line obtained from Langerhans islets is a cell line where at least one gene of the genes selected from the group consisting of preproinsulin gene, prepro-glucagon gene, preprosomatostatin gene, prepropancreatic polypeptide gene, prohormone convertase 1 (PC1) gene, prohormone convertase 2 (PC2) gene, glucagon-like peptide-1 (GLP-1) receptor gene, PDX1 (pancreatic-duodenal homeobox 1) gene, Pax 4 gene, Pax 6 gene, neurogenin 3 gene, neuro D gene, Nkx 2.2 gene, Nkx 6.1 gene, glucokinase gene, type 2 glucose transporter gene, beta-cellulin gene, sulfonylurea gene, $P2Y_1$ receptor gene, glucagon-like peptide-1 (GLP-1) receptor gene, type 1

somatostatin receptor gene, type 2 somatostatin receptor gene, type 3 somatostatin receptor gene, type 4 somatostatin receptor gene, type 5 somatostatin receptor gene, insulin receptor gene, glucose transporter gene and nestin gene is endogenously expressed.

34. The cell line according to claim 30 or 32, wherein the temperature-sensitive mutant strain of SV40 is SV40tsA58.

35. The cell line according to claim 31 or 32, wherein the non-human transgenic animal is a transgenic rat.

36. A process for producing a peptide, which comprises the following steps (1) and (2):

(1) culturing the cell line mentioned in any of claims 27 to 35 to produce and accumulate a peptide which is expressed by the cell endogenously, in the culture; and

(2) recovering the peptide from the culture obtained in the above (1).

37. A process for producing a peptide, which comprises the following steps (1) to (3):

(1) transfecting a DNA encoding an aimed peptide into a host cell to obtain a transformant wherein the cell line mentioned in any of claims 27 to 35 is used as the host cell;

(2) culturing the transformant to produce and accumulate a peptide in the culture; and

(3) recovering the peptide from the culture obtained in the above (2).

38. The process for producing a peptide according to claim 36 or 37, wherein culturing is carried out at the temperature where activity of the large T antigen of the temperature-sensitive mutant strain of SV40 is not suppressed.

39. The process for producing a peptide according to any of claims 36 to 38, which comprises a step for culturing in a serum-free medium, a medium containing not more than 2% of serum or a serum-free medium to which an N-supplement is added.

40. The process for producing a peptide according to any of claims 36 to 39, which comprises a step for culturing in a medium containing 5 to 30 mmol/L of glucose.

41. The process for producing a peptide according to any of claims 36 to 40, which comprises a step for culturing in a medium to which an agonist or antagonist for a receptor, a transporter or a channel expressed in the host cell is added.

42. The process for producing a peptide according to claim 41, wherein the receptor is G-protein coupled receptor, nuclear receptor, growth factor receptor, sulfonylurea receptor, ciliary neurotrophic factor receptor, leptin receptor, cytokine receptor or sulfonylurea receptor.

43. The process for producing a peptide according to claim 41, wherein the transporter is a glucose transporter.

44. The process for producing a peptide according to claim 41, wherein the channel is Ca channel, K channel, Cl channel or Na channel.

45. The process for producing a peptide according to any of claims 36 to 44, which comprises a step for culturing in a medium to which a substance capable of substituting a signal of a receptor expressed in a host cell is added.

46. The process for producing a peptide according to claim 45, wherein the substance capable of substituting the signal of the receptor is at least one substance selected from the group consisting of adenylate cyclase, protein kinase, phosphodiesterase, low-molecular G protein, substance capable of changing intracellular cAMP or intracellular Ca^{2+} content, forskolin, 8-bromo-cyclic AMP (8-Br-cAMP), phorbol 12-myristate 13-acetate (PMA), ionomycin and 3-isobutyl-1-methylxanthine.

47. The process for producing a peptide according to any of claims 36 to 46, which comprises a step for culturing on a dish coated with laminin or gelatin.

48. The process for producing a peptide according to any of claims 36 to 46, wherein culturing is carried out in a medium to which succinylated concanavalin A is added.

49. The process for producing a peptide according to any of claims 36 to 48, wherein culturing is carried out in a medium to which at least one substance selected from the group consisting of activin, glucagon-like peptide-1 (GLP-1), follistatin, glucose, hepatocyte growth factor, epidermal growth factor, nicotinamide, beta-cellulin, parathyroid

hormone-related peptide, thyrotropin-releasing hormone, vascular endothelial growth factor, islet neogenesis-associated protein, platelet-derived growth factor, insulin-like growth factor I, fibroblast growth factor, nerve growth factor and Reg protein is added.

50. The process for producing a peptide according to any of claims 36 to 49, wherein a secretagogue is added after an active peptide is produced and accumulated in the culture.

51. The process for producing a peptide according to claim 50, wherein the secretagogue is potassium, glucose, tolbutamide or ATP.

52. The process for producing a peptide according to any of claims 37 to 51, wherein DNA encoding one or more peptide(s) is introduced into a host cell to produce plural peptides.

53. A method of detecting or isolating a peptide capable of acting as an agonist, an antagonist or an inverse agonist for an aimed receptor, which comprises the following steps (1) to (4):

(1) isolating a DNA encoding a peptide capable of acting as an agonist, an antagonist or an inverse agonist for an aimed receptor by the method mentioned in any of claims 1 to 26;

(2) contacting the peptide encoded by the DNA or a partial peptide thereof with a cell where the aimed receptor is expressed;

(3) detecting a response reaction of the cell on the basis

of the receptor; and

(4) identifying the peptide or the partial peptide which gives a response reaction in the above (3).

54. A method of detecting or isolating a peptide capable of acting as an agonist, an antagonist or an inverse agonist for an aimed receptor, which comprises the following steps (1) to (4):

(1) preparing a peptide by the method of producing a peptide mentioned in any of claims 36 to 52;

(2) contacting the peptide with a cell where an aimed receptor is expressed;

(3) detecting a response reaction of the cell on the basis of the receptor; and

(4) identifying the peptide which gives a response reaction in the above (3).

55. The method of detecting or isolating a peptide according to claim 53 or 54, wherein the receptor is a G-protein coupled receptor.

56. The method of detecting or isolating a peptide according to claim 55, wherein the G-protein coupled receptor is an orphan G-protein coupled receptor.

57. The method of detecting or isolating a peptide according to claim 53 or 54, wherein the cell where the receptor is expressed is a B-cell line which is adapted for serum-free culture and in which the EBNA-1 gene of Epstein-Barr virus is

expressed, where at least one of the following (1) to (3) is integrated into a chromosomal DNA:

(1) DNA construct for expression of transcription factor necessary for construction of an inducible expression system;

(2) DNA construct where a reporter gene is ligated at the downstream area of promoter having a responsive element of a transcription factor; and

(3) DNA construct for expression of Gα protein or a chimeric Gα protein.

58. The method of detecting or isolating a peptide according to claim 57, wherein the B-cell line is a Namalwa cell adapted for serum-free culture.

59. The method of detecting or isolating a peptide according to claim 58, wherein a Namalwa cell adapted for serum-free culture is Namalwa KJM-1 cell.

60. The method of detecting or isolating a peptide according to claim 57, wherein the transcription factor necessary for construction of the inducible expression system is a chimeric protein of a ligand binding domain of estrogen receptor and yeast Gal4p.

61. The method of detecting or isolating a peptide according to claim 57, wherein the responsive element of the transcription factor is cAMP responsive element (CRE), TPA responsive element (TRE), NFAT (nuclear factor of activated T cells) responsive element or serum responsive element (SRE).

62. The method of detecting or isolating a peptide according to claim 57, wherein the reporter gene is firefly luciferase gene, *Renilla reniformis* luciferase gene, chloramphenicol acetyltransferase gene, β-galactosidase gene, β-lactamase gene or green fluorescent protein gene.

63. The method of detecting or isolating a peptide according to claim 57, wherein the Gα protein is at least one Gα protein selected from the group consisting of $G\alpha_{16}$, $G\alpha_{15}$, $G\alpha_q$, $G\alpha_{11}$, $G\alpha_s$, $G\alpha_i$, $G\alpha_o$, $G\alpha_z$, $G\alpha_{12}$, $G\alpha_{13}$, $G\alpha_{gust}$, $G\alpha_t$ and $G\alpha_{14}$.

64. The method of detecting or isolating a peptide according to claim 57, wherein the chimeric Gα protein is at least one chimeric Gα protein selected from the group consisting of the following (1) to (20):

(1) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_q$;

(2) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_i$;

(3) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_o$;

(4) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_z$;

(5) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_{12}$;

(6) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_{13}$;

(7) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_{gust}$;

(8) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_t$;

(9) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_{14}$;

(10) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_{16}$;

(11) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_s$;

(12) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_i$;

(13) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_o$;

(14) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_z$;

(15) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_{12}$;

(16) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_{13}$;

(17) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_{gust}$;

(18) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_t$;

(19) chimeric Gα protein where C-terminal 5 amino acids

of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_{14}$; and

(20) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_{16}$.

65. The method of detecting or isolating a peptide according to claim 57, wherein the transcription factor necessary for construction of the inducible expression system is a chimeric protein of a ligand binding domain of estrogen receptor and yeast Gal4p, the promoter having a responsive element of the transcription factor is a promoter having a cAMP responsive element (CRE) and the reporter gene is firefly luciferase gene or *Renilla reniformis* luciferase gene.

66. The method of detecting or isolating a peptide according to claim 57, wherein the transcription factor necessary for construction of the inducible expression system is a chimeric protein of a ligand binding domain of estrogen receptor and yeast Gal4p, the promoter having a responsive element of the transcription factor is a promoter having a cAMP responsive element (CRE), the reporter gene is firefly luciferase gene or *Renilla reniformis* luciferase gene and the chimeric Gα protein is a chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_q$ or a chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_i$.

67. The method of detecting or isolating a peptide according to claim 53 or 54, wherein the response reaction of the cell is at least one response reaction selected from the group consisting of release of arachidonic acid, release of acetylcholine, increase of intracellular Ca^{2+}, production of intracellular cAMP, decrease of intracellular cAMP, production of intracellular cGMP, production of inositol phosphate, change in cell membrane potential, phosphorylation of intracellular protein, activation of c-fos, change in intracellular pH, cell growth, expression level of reporter gene and expression level of marker gene.

68. A cell line derived from a B-cell line which is adapted for serum-free culture and in which the EBNA-1 gene of Epstein-Barr virus is expressed, where at least one of the following (1) to (3) is integrated into a chromosomal DNA:

(1) DNA construct for expression of a transcription factor necessary for construction of an inducible expression system;

(2) DNA construct where a reporter gene is ligated at the downstream area of a promoter having a responsive element of a transcription factor; and

(3) DNA construct for expression of Gα protein or a chimeric Gα protein.

69. The cell line according to claim 68, wherein the cell line is a Namalwa cell adapted for serum-free culture.

70. The cell line according to claim 69, wherein the Namalwa

cell adapted for serum-free culture is Namalwa KJM-1 cell.

71. The cell line according to claim 68, wherein the transcription factor necessary for construction of the inducible expression system is a chimeric protein of a ligand binding domain of estrogen receptor and yeast Gal4p.

72. The cell line according to claim 68, wherein the responsive element of the transcription factor is cAMP responsive element (CRE), TPA responsive element (TRE), NFAT (nuclear factor of activated T cells) responsive element or serum responsive element (SRE).

73. The cell line according to claim 68, wherein the reporter gene is firefly luciferase gene, *Renilla reniformis* luciferase gene, chloramphenicol acetyltransferase gene, β-galactosidase gene, β-lactamase gene or green fluorescent protein gene.

74. The cell line according to claim 68, wherein the Gα protein is at least one Gα protein selected from the group consisting of $G\alpha_{16}$, $G\alpha_{15}$, $G\alpha_{q}$, $G\alpha_{11}$, $G\alpha_{s}$, $G\alpha_{i}$, $G\alpha_{o}$, $G\alpha_{z}$, $G\alpha_{12}$, $G\alpha_{13}$, $G\alpha_{gust}$, $G\alpha_{t}$ and $G\alpha_{14}$.

75. The cell line according to claim 68, wherein the chimeric Gα protein is at least one chimeric Gα protein selected from the group consisting of the following (1) to (20):

(1) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_{s}$ are substituted with C-terminal 5 amino acids of $G\alpha_{q}$;

(2) chimeric Gα protein where C-terminal 5 amino acids

of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_i$;

(3) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_o$;

(4) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_z$;

(5) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_{12}$;

(6) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_{13}$;

(7) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_{gust}$;

(8) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_t$;

(9) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_{14}$;

(10) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_{16}$;

(11) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_s$;

(12) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_i$;

(13) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_o$;

(14) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_z$;

(15) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_{12}$;

(16) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_{13}$;

(17) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_{gust}$;

(18) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_t$;

(19) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_{14}$; and

(20) chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_q$ are substituted with C-terminal 5 amino acids of $G\alpha_{16}$.

76. The cell line according to claim 68, wherein the transcription factor necessary for construction of the inducible expression system is a chimeric protein of a ligand binding domain of estrogen receptor and yeast Gal4p, the promoter having a responsive element of the transcription factor is a promoter having a cAMP responsive element (CRE) and the reporter gene is firefly luciferase gene or *Renilla reniformis* luciferase gene.

77. The cell line according to claim 68, wherein the transcription factor necessary for construction of the inducible expression system is a chimeric protein of a ligand binding domain of estrogen receptor and yeast Gal4p, the promoter

having a responsive element of the transcription factor is a promoter having a cAMP responsive element (CRE), the reporter gene is firefly luciferase gene or *Renilla reniformis* luciferase gene and the chimeric Gα protein is a chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_q$ or a chimeric Gα protein where C-terminal 5 amino acids of $G\alpha_s$ are substituted with C-terminal 5 amino acids of $G\alpha_i$.

78. A method of isolating a DNA encoding a peptide capable of reacting with a substance to be tested, which comprises the following steps (1) to (4):

(1) transfecting a cDNA or a DNA derived from a chromosome into the cell line mentioned in any of claims 68 to 77 to obtain a transformant;

(2) measuring a response reaction of the transformant in the presence of the substance to be tested using the transformant in which the transfected cDNA or chromosomal DNA is expressed;

(3) measuring a response reaction of the transformant in the absence of the substance to be tested using the transformant in which the transfected cDNA or chromosomal DNA is expressed; and

(4) comparing the above response reactions (2) and (3), selecting the transformant showing different response reaction and identifying the DNA transfected in the transformant.

79. A method of isolating a DNA encoding a peptide capable of reacting with a substance to be tested, which comprises the following steps (1) to (7):

(1) dividing a cDNA library prepared using expression vector into pools each having 1 to 10,000 clone(s);

(2) transfecting a mixture of cDNA clones derived from each pool into a cell line mentioned in any of claims 68 to 77 to obtain a transformant;

(3) measuring a response reaction of the transformant in the presence of the substance to be tested for each pool using the transformant in which the transfected cDNA is expressed;

(4) measuring a response reaction of the transformant in the absence of the substance to be tested for each pool using the transformant in which the transfected cDNA is expressed;

(5) comparing the above response reactions of (3) and (4), selecting the pool showing different response reaction and dividing the selected pool into smaller pools than those in (1);

(6) repeating the operations of (2) to (5) until each pool consists of one clone; and

(7) identifying the transformant showing difference response reaction in the presence and the absence of the substance to be tested and identifying the DNA which is transfected in the transformant.

80. The method of isolating a DNA according to claim 78 or 79, wherein the response reaction of the cell is at least one response reaction selected from the group consisting of release of arachidonic acid, release of acetylcholine, increase of intracellular Ca^{2+}, production of intracellular cAMP, decrease of intracellular cAMP, production of intracellular cGMP, production of inositol phosphate, change in cell membrane potential, phosphorylation of intracellular protein, activation of c-fos, change in intracellular pH, cell growth, expression level of a reporter gene and expression level of a marker gene.

81. The method of isolating a DNA according to claim 78 or 79, wherein the substance to be tested is a substance which is prepared by culturing the cell line mentioned in any of claims 27 to 35.

82. The method of isolating a DNA according to any of claims 78 to 81, wherein culturing is carried out at the temperature where activity of large T antigen of temperature-sensitive mutant of SV40 is suppressed or disappeared.

83. A method of isolating a DNA encoding a peptide, which comprises the following steps (1) to (5):

(1) selecting a cell line where a DNA construct comprising a reporter gene ligated to downstream area of promoter having a response element of transcription factor is integrated in

chromosomal DNA, which is selected from the cell lines mentioned in any of claims 68 to 77, as a host cell;

(2) transfecting a cDNA or a DNA derived from a chromosome into the host cell to obtain a transformant;

(3) measuring the expression level of the reporter gene in the transformant obtained in the above (2) when the transfected cDNA or DNA is expressed;

(4) measuring the expression level of the reporter gene in the host cell or in the transformant obtained in the above (2) when the transfected cDNA or DNA is not expressed; and

(5) comparing the expression levels of the reporter gene in the above (3) and (4), selecting the transformant showing different expression level of the reporter gene, and identifying a DNA transfected in the transformant.

84. A method of isolating a DNA encoding a peptide, which comprises the following steps (1) to (8):

(1) dividing a cDNA library prepared using the inducible expression vector into pools each having 1 to 10,000 clone(s);

(2) selecting a cell line where DNA construct comprising a reporter gene ligated to downstream area of promoter having a response element of transcription factor is integrated in chromosomal DNA, which is selected from the cell lines mentioned in any of claims 68 to 77, as a host cell;

(3)transfecting a mixture of cDNA clones derived from each pool divided in the above (1) into the host cell obtained

in the above (2) to obtain a transformant for each pool;

(4) measuring the expression level of reporter gene in the transformant for each pool of the above (3) when the transfected cDNA is expressed;

(5) measuring the expression level of reporter gene in the transformant for each pool of the above (3) when the transfected cDNA is not expressed;

(6) comparing the expression levels of reporter genes in the above (4) and (5) for each pool, selecting the transformant showing higher expression level of reporter gene in (4) and dividing the selected pool into smaller pools than those in (1);

(7) repeating the operations of the above (2) to (6) until each pool consists of one clone; and

(8) identifying a transformant showing higher expression level of reporter gene in case the transfected cDNA is expressed than in case the transfected cDNA is not expressed and identifying the DNA transfected in the transformant.

85. The method of isolating a DNA according to claim 78, 79, 83 or 84, wherein the peptide is a receptor, a transcription factor, a signal transduction molecule or an enzyme.

86. The method of isolating a DNA according to claim 85, wherein the receptor is a G-protein coupled receptor.

87. The method of isolating a DNA according to claim 85, wherein the receptor is a constitutively activated G-protein

coupled receptor.

88. The method of isolating a DNA according to claim 86 or 87, wherein the G-protein coupled receptor is an orphan G-protein coupled receptor.

89. The method of isolating a DNA according to claim 78, 79, 83 or 84, wherein the peptide is a transcription factor, a signal transduction molecule or an enzyme, each of which has an activity to increase the activity of promoter having a responsive element of a transcription factor.

90. The method of isolating a DNA according to claim 78, 79, 83 or 84, wherein the cDNA is a cDNA with a random mutation, encoding a mutant G-protein coupled receptor, and the peptide is a constitutively activated G-protein coupled receptor.

91. The method of isolating a DNA according to claim 90, wherein the site into which the random mutation is introduced is from the second-half part of the third transmembrane region to the first-half part of the second intracellular region, or from the second-half part of the third intracellular region to the first-half part of the sixth transmembrane region in the G-protein coupled receptor.

92. The method of isolating a DNA according to claim 90 or 91, wherein the site into which the random mutation is introduced is an amino acid which is the 20th residue or the 22nd residue directed to the N-terminal side from a proline

residue existing in the sixth transmembrane region, in which the proline residue is one of conserved amino acid residues in a G-protein coupled receptor, or an amino acid residue corresponding to the proline residue.

93. A constitutively activated mutant G-protein coupled receptor which is isolated by the method mentioned in any of claims 90 to 92.

94. A constitutively activated mutant G-protein coupled receptor having a mutation at an amino acid which is the 20th residue or the 22nd residue directed to the N-terminal side from a proline residue existing in the sixth transmembrane region, in which the proline residue is one of conserved amino acid residues in a G-protein coupled receptor, or an amino acid residue corresponding to the proline residue.

95. A constitutively activated mutant G-protein coupled receptor selected from the group consisting of a constitutively activated mutant G-protein coupled receptor where the 221st serine from N terminal of OGR1 is substituted with asparagine; a constitutively activated mutant G-protein coupled receptor where the 118th aspartic acid from N terminal of OGR1 is substituted with alanine; a constitutively activated mutant G-protein coupled receptor where the 118th aspartic acid from N terminal of OGR1 is substituted with alanine and serine which is the 221st one is substituted with asparagine; a constitutively activated mutant G-protein coupled receptor where the 124th

aspartic acid from N terminal of RE2 is substituted with alanine; a constitutively activated mutant G-protein coupled receptor where the 113th aspartic acid from N terminal of GPR35 is substituted with alanine; a constitutively activated mutant G-protein coupled receptor where the 111th aspartic acid from N terminal of GPCR25 is substituted with alanine; a constitutively activated mutant G-protein coupled receptor where the 135th glutamic acid from N terminal of PGMO334 is substituted with phenylalanine, glutamine or alanine; a constitutively activated mutant G-protein coupled receptor where the 259th aspartic acid from N terminal of PGMO334 is substituted with serine; a constitutively activated mutant G-protein coupled receptor where the 217th arginine from N-terminal of GPR43 is substituted with proline; and a constitutively activated mutant G-protein coupled receptor where the 217th arginine and the 106th glutamic acid from N-terminal of GPR43 is substituted with proline and aspartic acid, respectively.

96. A method of screening or isolating an antagonist for MC1R using a type 1 melanocortin receptor (MC1R) and proadrenomedullin N-20 terminal peptide (PAMP) or a peptide consisting of the 9th to 20th amino acid residues from N-terminal of PAMP.

97. A method of screening or isolating an antagonist for GPR43 using an orphan G-protein coupled receptor GPR43 and acetic

acid, propionic acid, acetate or propionate.

98. A method of screening or isolating an antagonist for GPR41 using an orphan G-protein coupled receptor GPR41 and cyclopropanecarboxylic acid, propionic acid, cyclopropanecarboxylate or propionate.

99. A method of screening or isolating an antagonist for G10d using an orphan G-protein coupled receptor G10d and an α-melanocyte stimulating hormone or adrenocorticotropic hormone.

100. A method of isolating an agonist for a G-protein coupled receptor, which comprises the following steps (1) to (4):

(1) transfecting a DNA encoding a G-protein coupled receptor into the cell line mentioned in any of claims 68 to 77 to obtain a transformant;

(2) measuring a response reaction of the transformant in the presence of a substance to be tested using the transformant in which the transfected DNA is expressed;

(3) measuring a response reaction of the transformant in the absence of a substance to be tested using the transformant in which the transfected DNA is expressed; and

(4) comparing the response reactions of the above (2) and (3) and isolating the substance to be tested which induces the changes in the response reaction as an agonist.

101. A method of isolating an antagonist for a G-protein

coupled receptor, which comprises the following steps (1) to (4):

(1) transfecting a DNA encoding a G-protein coupled receptor into the cell line mentioned in any of claims 68 to 77 to obtain a transformant;

(2) measuring a response reaction of the transformant in the presence of an agonist for the G-protein coupled receptor using the transformant in which the transfected DNA is expressed;

(3) measuring a response reaction of the transformant in the presence of both an agonist for the G-protein coupled receptor and a substance to be tested using the transformant in which the transfected DNA is expressed; and

(4) isolating the substance to be tested which disappears the response reaction on the basis of the agonist of the transformant as an antagonist.

102. The method of isolating an agonist or an antagonist for a G-protein coupled receptor according to claim 100 or 101, wherein the response reaction of the cell is at least one response reaction selected from the group consisting of release of arachidonic acid, release of acetylcholine, increase of intracellular Ca^{2+}, production of intracellular cAMP, decrease of intracellular cAMP, production of intracellular cGMP, production of inositol phosphate, change in cell membrane potential, phosphorylation of intracellular protein, activation of c-fos, change in intracellular pH, cell growth,

expression level of reporter gene and expression level of marker gene.

103. A method of isolating an antagonist or inverse agonist for a G-protein coupled receptor, which comprises the following steps (1) to (5):

(1) selecting a cell line where a DNA construct comprising a reporter gene ligated to downstream area of promoter having a response element of transcription factor is integrated in chromosomal DNA, which is selected from the cell lines mentioned in any of claims 68 to 77, as a host cell;

(2) transfecting a DNA encoding a constitutively activated G-protein coupled receptor into the host cell to obtain a transformant;

(3) measuring the expression level of a reporter gene in the transformant in which the transfected DNA is expressed in the absence of a substance to be tested;

(4) measuring the expression level of a reporter gene in the transformant in which the transfected DNA is expressed in the presence of a substance to be tested; and

(5) comparing the expression levels of the reporter gene of the above (3) and (4) and isolating a substance to be tested which decrease the expression level of the reporter gene as an antagonist or an inverse agonist for the G-protein coupled receptor of (2).

104. A method of isolating an activator or inhibitor for

a peptide selected from the group consisting of transcription factors, signal transduction molecules and enzymes, which comprises the following steps (1) to (4):

(1) transfecting a DNA encoding a peptide selected from the group consisting of transcription factors, signal transduction molecules and enzymes into the cell line mentioned in any of claims 68 to 77 to obtain a transformant;

(2) measuring a response reaction of the transformant in the absence of a substance to be tested using the transformant in which the transfected DNA is expressed;

(3) measuring a response reaction of the transformant in the presence of a substance to be tested using the transformant in which the transfected DNA is expressed; and

(4) comparing the response reactions of the above (2) and (3) and isolating the substance to be tested which changes the response reaction as an activator or an inhibitor for the peptide.

105. The method of isolating an activator or inhibitor according to claim 104, wherein the response reaction of the cell is at least one response reaction selected from the group consisting of release of arachidonic acid, release of acetylcholine, increase of intracellular Ca^{2+}, production of intracellular cAMP, decrease of intracellular cAMP, production of intracellular cGMP, production of inositol phosphate, change in cell membrane potential, phosphorylation of intracellular

protein, activation of c-fos, change in intracellular pH, cell growth, expression level of reporter gene and expression level of marker gene.

106. A host-vector system which is characterized in that a cell line mentioned in any of claims 68 to 77 is used as a host cell and an expression vector having a promoter and oriP of Epstein-Barr virus is used as a vector.

107. The host-vector system according to claim 106, wherein the promoter is a Gal4p-responsible inducible expression promoter.

108. The host-vector system according to claim 106 or 107, wherein the expression vector is pAMo, pAMo-nd, pAMo-d, pAGal9-nd or pAGal9-d.